

**NUCLEIC ACID SEQUENCING BY RAMAN MONITORING OF UPTAKE OF
NUCLEOTIDES DURING MOLECULAR REPLICATION**

ABSTRACT OF THE DISCLOSURE

The methods and apparatus disclosed herein are useful for detecting nucleotides, nucleosides, and bases and for nucleic acid sequence determination. The methods involve detection of a nucleotide, nucleoside, or base using surface enhanced Raman spectroscopy (SERS) or surface enhanced coherent anti-Stokes Raman spectroscopy (SECARS). The detection can be part of a nucleic acid sequencing reaction to detect uptake of a deoxynucleotide triphosphate during a nucleic acid polymerization reaction, such as a nucleic acid sequencing reaction. The nucleic acid sequence of a synthesized nascent strand, and the complementary sequence of the template strand, can be determined by tracking the order of incorporation of nucleotides during the polymerization reaction. Methods for enhancing the SERS signal of a nucleotide or nucleoside by cleaving the base from a sugar moiety are provided. Furthermore, methods for detecting single base repeats are provided.